1: Vaccine. 2008 Aug 5;26(33):4224-30. Epub 2008 Jun 6. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Immunogenicity and efficacy of two candidate human metapneumovirus vaccines in cynomolgus macaques.

Herfst S, Schrauwen EJ, de Graaf M, van Amerongen G, van den Hoogen BG, de Swart RL, Osterhaus AD, Fouchier RA.

Department of Virology, Erasmus MC, Rotterdam, The Netherlands.

Human metapneumovirus (HMPV) is an important cause of acute respiratory tract disease for which the development of vaccine candidates is warranted. We have previously described the generation of an iscom matrix-adjuvanted HMPV fusion protein subunit vaccine (Fsol) and a live-attenuated vaccine (HMPVM11). Here, we evaluate the immunogenicity and efficacy of these vaccines in cynomolgus macaques. Immunization with Fsol induced HMPV F-specific antibody responses, virus neutralizing antibody titers, and cellular immune responses, but the induced humoral immune response waned rapidly over time. HMPVM11 was strongly attenuated and displayed limited immunogenicity, although immunization with this virus primed for a good secondary HMPV-specific lymphoproliferative response after challenge infection. The duration of virus shedding in HMPVM11-immunized animals was reduced compared to sham-immunized animals. Both vaccines induced HMPV-specific immune responses, but the rapid waning of immunity is a challenging obstacle for vaccine development.

PMID: 18585830 [PubMed - indexed for MEDLINE]

2: Microb Pathog. 2008 Feb;44(2):164-8. Epub 2007 Aug 21. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Protection afforded against aerosol challenge by systemic immunisation with inactivated Francisella tularensis live vaccine strain (LVS).

Eyles JE, Hartley MG, Laws TR, Oyston PC, Griffin KF, Titball RW.

Defence Science and Technology Laboratory, Porton Down, Salisbury, UK. jeeyles@dstl.gov.uk

BALB/c mice were immunised with inactivated Francisella tularensis live vaccine strain (LVS) and the level of protection afforded against aerosol challenge with virulent strains of F. tularensis ascertained. Intramuscular (IM) injection of inactivated LVS with an aluminium-hydroxide-based adjuvant-stimulated IgG1-biased LVS-specific antibody responses and afforded no protection against aerosol challenge with subspecies holarctica (strain HN63). Conversely, IM injection of inactivated LVS adjuvanted with preformed immune-stimulating complexes (ISCOMS) admixed with immunostimulatory CpG oligonucleotides afforded robust protection against aerosol-initiated infection with HN63. However, despite a significantly extended time-to-death relative to naïve controls, the majority of mice immunised with the most potent vaccine formulation were not protected against a low-dose aerosol challenge with subspecies tularensis (strain Schu S4). These data indicate that parenterally administered non-living vaccines can be used for effective immunisation against aerosol challenges with subspecies holarctica, although not high virulence strains of F. tularensis.

PMID: 17904793 [PubMed - indexed for MEDLINE]

3: Proteomics. 2007 Jun;7(13):2172-83. Related Articles, Links

FULL TEXT AVAILABLE ONLINE Wiley InterScience

Immunodominant Francisella tularensis antigens identified using proteome microarray. Crown Copyright 2007 Dstl.

Eyles JE, Unal B, Hartley MG, Newstead SL, Flick-Smith H, Prior JL, Oyston PC, Randall A, Mu Y, Hirst S, Molina DM, Davies DH, Milne T, Griffin KF, Baldi P, Titball RW, Felgner PL.

Defence Science and Technology Laboratory, Porton Down, Salisbury, UK. jeeyles@dstl.gov.uk

Stimulation of protective immune responses against intracellular pathogens is difficult to achieve using non-replicating vaccines. BALB/c mice immunized by intramuscular injection with killed Francisella tularensis (live vaccine strain) adjuvanted with preformed immune stimulating complexes admixed with CpG, were protected when systemically challenged with a highly virulent strain of F. tularensis (Schu S4). Serum from immunized mice was used to probe a whole proteome microarray in order to identify immunodominant antigens. Eleven out of the top 12 immunodominant antigens have been previously described as immunoreactive in F. tularensis. However, 31 previously unreported immunoreactive antigens were revealed using this approach. Twenty four (50%) of the ORFs on the immunodominant hit list belonged to the category of surface or membrane associated proteins compared to only 22% of the entire proteome. There were eight hypothetical protein hits and eight hits from proteins associated with different aspects of metabolism. The chip also allowed us to readily determine the IgG subclass bias, towards individual or multiple antigens, in protected and unprotected animals. These data give insight into the protective immune response and have potentially important implications for the rational design of non-living vaccines for tularemia and other intracellular pathogens.

PMID: 17533643 [PubMed - indexed for MEDLINE]

4: Vaccine. 2006 Mar 20;24(13):2302-16. Epub 2005 Dec 1. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Low titer maternal antibodies can both enhance and suppress B cell responses to a combined live attenuated human rotavirus and VLP-ISCOM vaccine.

Nguyen TV, Yuan L, P Azevedo MS, Jeong KI, Gonzalez AM, Iosef C, Lovgren-Bengtsson K, Morein B, Lewis P, Saif LJ.

Food Animal Health Research Program, Department of Veterinary Preventive Medicine, Ohio Agricultural Research and Development Center, The Ohio State University, 1680 Madison Avenue, Wooster, OH 44691-4096, USA.

We investigated effects of low titer (Lo) circulating MatAb on protection and immunogenicity of attenuated (Att) human rotavirus (HRV) priming and 2/6-virus-like particle (VLP)-immunostimulating complex (ISCOM) boosting (AttHRV/VLP) or VLP-ISCOM alone vaccines. LoMatAb had both enhancing and suppressing effects on B cell responses, depending on tissue, antibody isotype and vaccine. Differential effects of LoMatAb on IgA responses in different tissues suggest that LoMatAb did not suppress induction of IgA effector and memory B cells but impaired homing of these cells to secondary lymphoid or effector tissues, reducing IgA antibody secreting cells and antibodies at these sites. The AttHRV/VLP vaccine partially overcame LoMatAb suppression, conferred moderate protection against virulent HRV (as measured by reduced viral shedding and diarrhea) and represents a new candidate for rotavirus vaccines for both humans and animals.

Publication Types:
- Research Support, N.I.H., Extramural
- Research Support, U.S. Gov't, Non-P.H.S.

PMID: 16361002 [PubMed - indexed for MEDLINE]

5: Vet Immunol Immunopathol. 2005 Dec 15;108(3-4):345-55. Epub 2005 Aug 10. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

The use of a systemic prime/mucosal boost strategy with an equine influenza ISCOM vaccine to induce protective immunity in horses.

Crouch CF, Daly J, Henley W, Hannant D, Wilkins J, Francis MJ.

Schering-Plough Animal Health, Breakspear Road South, Harefield, Uxbridge, Middlesex UB9 6LS, UK. olin.crouch@spcorp.com

In horses, natural infection confers long lasting protective immunity characterised by mucosal IgA and humoral IgGa and IgGb responses. In order to investigate the potential of locally administered vaccine to induce a protective IgA response, responses generated by vaccination with an immunostimulating complex (ISCOM)-based vaccine for equine influenza (EQUIP F) containing A/eq/Newmarket/77 (H7N7), A/eq/Borlänge/91 (H3N8) and A/eq/Kentucky/98 (H3N8) using a systemic prime/mucosal boost strategy were studied. Seven ponies in the vaccine group received EQUIP F vaccine intranasally 6 weeks after an initial intramuscular immunisation. Following intranasal boosting a transient increase in virus-specific IgA was detected in nasal wash secretions. Aerosol challenge with the A/eq/Newmarket/1/93 reference strain 4 weeks after the intranasal booster resulted in clinical signs of infection and viral shedding in seven of seven influenza-naive control animals whereas the seven vaccinated ponies had statistically significantly reduced clinical signs and duration of virus excretion. Furthermore, following this challenge, significantly enhanced levels of virus-specific IgA were detected in the nasal washes from vaccinated ponies compared with the unvaccinated control animals. These data indicate that the intranasal administration of EQUIP F vaccine primes the mucosal system for an enhanced IgA response following exposure to live influenza virus.

PMID: 16098611 [PubMed - indexed for MEDLINE]

6: Clin Exp Immunol. 2004 Mar;135(3):361-72. Related Articles, Links

FULL TEXT AVAILABLE ONLINE WILEY InterScience® FREE full text article in PubMed Central

Antibody responses to human rotavirus (HRV) in gnotobiotic pigs following a new prime/boost vaccine strategy using oral attenuated HRV priming and intranasal VP2/6 rotavirus-like particle (VLP) boosting with ISCOM.

González AM, Nguyen TV, Azevedo MS, Jeong K, Agarib F, Iosef C, Chang K, Lovgren-Bengtsson K, Morein B, Saif LJ.

Food Animal Health Research Program, Ohio Agricultural Research and Development Center, Department of Veterinary Preventive Medicine, The Ohio State University, OH 44691, USA.

Safer and more effective human rotavirus (HRV) vaccines are needed. We evaluated oral priming with attenuated WaHRV (AttHRV) followed by boosting with two intranasal (IN) doses of VP2/6 virus-like particles (2/6 VLP) with immunostimulating complexes (ISCOM) to determine if this regimen induces protection against diarrhoea and viral shedding in the gnotobiotic pig model. IgM, IgA and IgG antibody titres in serum and intestinal contents were quantified by enzyme-linked immunosorbent assay (ELISA) and serum neutralizing antibody titres were measured by a virus neutralization (VN) test. Seven groups of neonatal gnotobiotic pigs were vaccinated at post-inoculation days (PID) 0, 10 and 21 and challenged with virulent WaHRV at PID 28. The vaccine groups included: (1, 2) oral priming with AttHRV and boosting with two IN immunizations with 2/6 VLP-ISCOM (Att + 2/6 VLP-ISCOM) at VLP concentrations of 250 micro g or 25 micro g; (3, 4) three IN immunizations with 2/6 VLP-ISCOM at VLP concentrations of 250 micro g or 25 micro g (2/6 VLP-ISCOM); (5) three oral immunizations with AttHRV (3xAttHRV); (6) one oral immunization with AttHRV (1xAttHRV); (7) controls (ISCOM matrix and/or diluent). The pigs that received 3xAttHRV or Att + 2/6 VLP250-ISCOM had the highest protection rates against diarrhoea upon challenge at PID 28 with virulent WaHRV. The IgA antibody titres to HRV in intestinal contents were significantly higher in the Att + 2/6 VLP250-ISCOM group than in all other groups prechallenge

(PID 28). Serum VN antibody titres were statistically similar after the first inoculation among the groups given AttHRV, but at PID 28 VN antibody titres were significantly higher for the 3xAttHRV and Att + 2/6 VLP250-ISCOM groups than for the 1xAttHRV group suggesting that boosting with 2/6 VLP also boosted VN antibody responses. In humans, intestinal IgA antibodies have been correlated with protection against symptomatic reinfection. Thus the vaccine regimen of one oral dose of AttHRV and two IN immunizations with 2/6 VLP250-ISCOM may be an alternative to multiple-dose live oral vaccines in humans.

Publication Types:
- Research Support, U.S. Gov't, P.H.S.

PMID: 15008967 [PubMed - indexed for MEDLINE]

PMCID: PMC1808978

7: Int J Parasitol. 2002 Jun 15;32(7):867-76. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Immunisation of mice against neosporosis.

Lundén A, Wright S, Allen JE, Buxton D.

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In the present study a murine encephalitis model was used to investigate if protection against neosporosis could be achieved by immunisation. Groups of 10 mice were immunised with a sublethal dose of live Neospora caninum tachyzoites, N. caninum antigens incorporated into iscoms, N. caninum lysate mixed with Quil A, or N. caninum lysate in PBS. Control mice were given Quil A only. Challenge infection with 2.5x10(6) N. caninum tachyzoites resulted in clinical symptoms that remained until the end of the experiment in the controls. In contrast, mice immunised with live parasites or parasite lysate in Quil A only showed mild and transient symptoms. Of nine mice immunised with N. caninum iscoms, seven recovered while two died. Most severely affected were the mice immunised with parasite lysate only; all of them died within 28 days post-infection. Histological examination and scoring of brain lesions gave a significantly lower ($P<0.0001$) lesion score in mice immunised with live parasites than in controls. The groups immunised with iscoms or lysate and Quil A also had reduced lesion scores ($P<0.04$ and 0.07, respectively) but not the group given parasite lysate alone. The lesions seen in the latter group differed from those in the other groups. There was less cellular reaction and more tachyzoites indicating an active infection. The N. caninum specific antibody responses and cytokine production (IFN-gamma, IL-4 and IL-5) of splenocytes were analysed at the time of challenge infection. The results suggest a correlation between protection and high levels of IFN-gamma. Also, the immune responses recorded in mice immunised with parasite lysate without adjuvant were relatively weak and more towards the Th2 type, when compared with the other immunisation schedules. This is consistent with the weaker inflammatory response observed in the brains of these mice.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 12062558 [PubMed - indexed for MEDLINE]

8: Vaccine. 2002 Mar 15;20(13-14):1741-53. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Systemic and intestinal antibody secreting cell responses and protection in gnotobiotic pigs immunized orally with attenuated Wa human rotavirus and Wa 2/6-rotavirus-like-particles associated with immunostimulating complexes.

Iosef C, Van Nguyen T, Jeong K, Bengtsson K, Morein B, Kim Y, Chang KO, Azevedo MS, Yuan L, Nielsen P, Saif LJ.

Food Animal Health Research Program, Department of Veterinary Preventive Medicine, Ohio Agricultural Research and Development Center, The Ohio State University, 1680 Madison Avenue, Wooster, OH 44691-4096, USA.

The undesirable side effects and variable efficacy of some oral live rotavirus vaccines in infants have necessitated alternative vaccine approaches. We evaluated a recombinant RFVP2/WaVP6 rotavirus-like-particle (2/6VLP) oral vaccine, using an immunostimulating complex (ISCOM) matrix as adjuvant, in a gnotobiotic (Gn) pig model of human rotavirus (HRV) disease. The 2/6VLPs adhered to the ISCOM-matrix (2/6VLP-ISCOM) and were antigenic, but they failed to induce protection. However, when combined with attenuated (Att) HRV for oral priming, the 2/6VLP-ISCOM vaccine was effective as a booster and induced partial protection against virulent Wa HRV. The 250 microg 2/6VLP dose was more effective than 100 microg. The highest mean numbers of IgA antibody secreting cells evaluated by ELISPOT in intestinal lymphoid tissues were in pigs receiving AttHRV+2/6VLP-ISCOM or three doses of AttHRV and were associated with the highest protection rates.

Publication Types:
- Research Support, Non-U.S. Gov't
- Research Support, U.S. Gov't, Non-P.H.S.
- Research Support, U.S. Gov't, P.H.S.

PMID: 11906761 [PubMed - indexed for MEDLINE]

9: FEMS Immunol Med Microbiol. 2001 Aug;31(2):105-12. Related Articles, Links

FULL TEXT AVAILABLE ONLINE WILEY InterScience

Different respiratory syncytial virus and Quillaja saponin formulations induce murine peritoneal cells to express different proinflammatory cytokine profiles.

Hu KF, **Chen M**, **Abusugra I**, **Monaco F**, **Morein B**.

Faculty of Veterinary Medicine, Department of Veterinary Microbiology, Swedish University of Agricultural Sciences, Uppsala, Sweden.

The recognition of a pathogen or a vaccine antigen formulation by cells in the innate immune system leads to production of proinflammatory cytokines, which will determine the ensuing acquired immune response quantitatively and qualitatively. Tumour necrosis factor (TNF)-alpha, interleukin (IL)-1 and IL-6 are the first set of cytokines produced upon such an encounter, which have roles both in protective immunity and immunopathogenesis evident with respiratory syncytial virus (RSV). RSV antigens in different physical adjuvant-vaccine formulations were analysed for their capacity to provoke cultured murine peritoneal cells to produce these three proinflammatory cytokines. RSV immunostimulating complex (ISCOM), i.e. both antigen and adjuvant are incorporated in the same particle, induced high levels of IL-1alpha being of the same magnitude or higher than those of live RSV and lipopolysaccharide (LPS). Live virus and LPS induced higher levels of IL-6 and TNF-alpha than ISCOM and so did non-adjuvanted UV-inactivated RSV but only at high doses. ISCOM-Matrix, i.e. ISCOM without antigens, admixed as a separate entity to inactivated RSV, downregulated or blocked the cytokine response to the inactivated RSV in contrast to ISCOM. Kinetic studies showed that ISCOM induced cytokine production first detected at hours 1, 2, 4 for TNF-alpha, IL-6 and IL-1alpha respectively, which was earlier than for the other antigen formulations containing corresponding doses of antigen and/or Quillaja adjuvant. Peak values for production of TNF-alpha and IL-6 were at 8 h and for IL-1alpha at 72 h following stimulation with ISCOM. The delayed appearance of IL-1alpha may reflect the cell-bound nature of this cytokine.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 11549417 [PubMed - indexed for MEDLINE]

10: Vaccine. 2001 Jul 16;19(28-29):4072-80. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Intranasal immunisation with influenza-ISCOM induces strong mucosal as well as systemic antibody and cytotoxic T-lymphocyte responses.

Sjölander S, Drane D, Davis R, Beezum L, Pearse M, Cox J.

CSL Limited, Immunology Research & Development, Parkville, Vic. 3052, Australia.

Intranasal administration of vaccines is preferred for induction of mucosal immune responses. In this study, mice were immunised intranasally and subcutaneously with influenza-immuno stimulating complexes (influenza-ISCOM). The intranasal dose was 15-times the subcutaneous dose. All mice dosed with influenza-ISCOMs survived challenge with live virus and comparable serum antibody and splenic cytotoxic T-lymphocyte responses were detected in both groups. Induction of mucosal IgA was significantly higher with intranasal immunisation and was comparable to responses induced with the heat labile enterotoxin of Escherichia coli as adjuvant. These findings demonstrate that intranasal administration of high dose influenza-ISCOM results in potent systemic and mucosal immune responses.

PMID: 11427284 [PubMed - indexed for MEDLINE]

11: Infect Immun. 2000 Jun;68(6):3074-8. Related Articles, Links

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Priming with Chlamydia trachomatis major outer membrane protein (MOMP) DNA followed by MOMP ISCOM boosting enhances protection and is associated with increased immunoglobulin A and Th1 cellular immune responses.

Dong-Ji Z, Yang X, Shen C, Lu H, Murdin A, Brunham RC.

Department of Medical Microbiology, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba R3E OW3.

We previously reported that DNA vaccination was able to elicit cellular immune responses and partial protection against Chlamydia trachomatis infection. However, DNA immunization alone did not generate immune responses or protection as great as that induced by using live organisms. In this study, we evaluated the immunologic effects of a combinational vaccination approach using C. trachomatis mouse pneumonitis (MoPn) major outer membrane protein (MOMP) DNA priming followed by boosting with immune-stimulating complexes (ISCOM) of MOMP protein (MOMP ISCOM) for protection of BALB/c mice against MoPn lung infection. Substantially better protection to challenge infection was observed in mice given combinational vaccination compared with mice given MOMP ISCOM immunization alone, and the protection approximated that induced by live organisms. Enhanced protection was correlated with stronger delayed-type hypersensitivity, higher levels of gamma interferon production, and increased immunoglobulin A antibody responses in lung homogenates. The results indicate that DNA priming followed by ISCOM protein boosting may be useful in designing a fully protective chlamydial vaccine.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 10816446 [PubMed - indexed for MEDLINE]

PMCID: PMC97534

12: Vaccine. 1998 Dec;16(20):2058-68. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Immunopotentiation of humoral and cellular responses to inactivated influenza vaccines by two different adjuvants with potential for human use.

Deliyannis G, Jackson DC, Dyer W, Bates J, Coulter A, Harling-McNabb L, Brown LE.

Department of Microbiology and Immunology, University of Melbourne, Parkville, Australia.

Two quite different adjuvants, currently under development for use in humans, have been examined for their effects on the magnitude and type of immunity elicited in response to inactivated influenza vaccine. Immunostimulating complexes (ISCOM adjuvant) contain the saponin ISCOPREP 703, and SPT is an oil-in-water emulsion of squalane, non-ionic block copolymer (L121) and Tween 80. Influenza virus vaccines formulated in either adjuvant were far superior to the non-adjuvanted aqueous vaccine in eliciting antibody and T-cell responses in mice, particularly at lower doses of antigen. In addition, the vaccines containing adjuvant were superior in eliciting protective immunity. One of the shortcomings of the unadjuvanted inactivated influenza vaccine was its inability to elicit a primary proliferative T-cell response. However, after one dose of either adjuvanted vaccine, strong proliferative responses were achieved. We also show that subcutaneous vaccination with inactivated vaccines is capable of modulating the isotype profile of antibody secreting cells generated in the lungs of mice in response to intranasal challenge with live virus. In this system, the isotype of antibody elicited after challenge of mice that had received ISCOM vaccine more closely mimicked that of animals vaccinated with live virus.

Publication Types:
- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 9796065 [PubMed - indexed for MEDLINE]

13: Vaccine. 1998 Aug-Sep;16(14-15):1479-81. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Vaccine strategies to overcome maternal antibody mediated inhibition of measles vaccine.

Osterhaus A, van Amerongen G, van Binnendijk R.

Institute of Virology, Erasmus University Rotterdam, The Netherlands.

A vaccine that is effective in the presence of maternally derived virus neutralizing antibodies and can be administered successfully at an early age, would be favoured over the presently used live attenuated measles vaccines. With the advent of new molecular and immunological techniques, several options for the development of new generation vaccines, fulfilling these criteria, have arisen. We have recently evaluated the efficacy of recombinant vaccinia virus- and iscom-based candidate vaccines, presenting the F and H proteins of measles virus, in macaques with passively transferred virus neutralizing macaque antibodies. The data indicate that the further exploration of the potential of iscom based measles vaccines should be encouraged.

Publication Types:
- Review

PMID: 9711792 [PubMed - indexed for MEDLINE]

14: Vaccine. 1998 May-Jun;16(9-10):885-92. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

ISCOMs vaccine against experimental leishmaniasis.

Papadopoulou G, Karagouni E, Dotsika E.

Hellenic Pasteur Institute, Athens, Greece.

The major surface glycoprotein (gp63) of Leishmania major incorporated into the immunostimulating complexes (ISCOMs) was used to protect Balb/c mice against experimental infection. Two intraperitoneal vaccinations with low doses of gp63 into ISCOMs (gp63-ISCOMs) induced protective immunity in vaccinated mice as indicated by reduced inflammation and suppressed lesions after experimental challenge. An augmented IgG-specific secretion and a specific switching towards the IgG2a isotype was observed in the serum of vaccinated mice. Gp63-ISCOMs primed spleen cells restimulated in vitro with

soluble Leishmania antigen (SLA) or live parasites displayed strong gp63-specific proliferative responses and secreted high levels of interleukin-2, interferon gamma and interleukin-10 but not interleukin-4. No delayed type hypersensitivity response to either SLA or LV39 was detected. These data indicate that gp63-ISCOMs induced a protective immunity in the susceptible Balb/c mice against Leishmania challenge, modulating the immune response towards a Th1 rather than Th2 type.

Publication Types:
- In Vitro

PMID: 9682333 [PubMed - indexed for MEDLINE]

15: Vet Microbiol. 1997 Jun 16;56(3-4):213-25. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Assessment of the immunogenic potential of Rhodococcus equi virulence associated protein (VapA) in mice.

Prescott JF, **Patterson MC**, **Nicholson VM**, **Morein B**, **Yager JA**.

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The development of immunity to Rhodococcus equi, particularly to a virulence-associated protein (VapA) based antigen preparation, was examined in CD1 and BALB/c mice after intraperitoneal vaccination. Immunization with VapA based antigen without adjuvant markedly enhanced organ clearance in CD1 mice but not in BALB/c mice. Delayed type hypersensitivity response and antibody titres in VapA based antigen immunized BALB/c mice were less than in CD1 mice. By contrast also to CD1 mice, sera from immunized BALB/c mice did not react as strongly with VapA in western blots. Use of adjuvants (aluminium hydroxide, iscoms) interfered markedly with the immunogenic properties of the VapA based antigen, in the case of aluminium hydroxide by apparently driving a Th2 type of response. Unexpectedly, iscom adjuvants also impaired immunity and, despite the highest DTH response, produced a low IgG2a response, suggesting that iscomization of the antigen produced a low interferon gamma and high interleukin 2 response. Passive immunization of BALB/c mice with serum from mice immunized with live virulent strain 103+ resulted in only temporary and slight enhancement of organ clearance, supporting the central importance of cellular immunity to R. equi. Immunization with live virulence plasmid- and VapA-positive R. equi strain 103 resulted in marked liver clearance, in marked DTH response and high antibody titres. By contrast, immunization with live virulence plasmid- and VapA-negative strain 103 resulted in slight but variable enhancement of clearance, but insignificant DTH and antibody. The virulence plasmid, and by implication VapA, was thus shown to be critical in determining a highly effective protection to live organisms.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 9226836 [PubMed - indexed for MEDLINE]

16: Mech Ageing Dev. 1997 Jun;96(1-3):157-69. Related Articles, Links

Influenza (H1N1)-ISCOMs enhance immune responses and protection in aged mice.

Sambhara S, **Woods S**, **Arpino R**, **Kurichh A**, **Tamane A**, **Bengtsson KL**, **Morein B**, **Underdown B**, **Klein M**, **Burt D**.

Pasteur Merieux Connaught Canada, North York, Ontario, Canada.

Aging is associated with a decline in immune function and the elderly are therefore more susceptible to infectious disease and less responsive to vaccination. Influenza antigens complexed as immunostimulatory complexes (ISCOMs) generate more potent protective immune responses compared with non-adjuvanted flu antigens in young adult mice. We report on the protective efficacy of flu-ISCOMs compared with the current split flu vaccine in an aged mouse model. DBA/2 mice aged 2 or 18 months were immunized with

flu vaccine, ISCOMs or live virus, prior to challenge with the homologous virus. In aged mice, flu-ISCOMs induced significantly higher serum hemagglutination inhibition (HAI) titers compared to vaccine, similar to the levels obtained in young adult mice that received the split vaccine. Flu-ISCOMs but not vaccine induced cytotoxic T lymphocyte (CTL) responses in young and to a lesser degree in aged mice. In aged mice flu-ISCOMs significantly reduced illness and enhanced recovery from viral infection compared with vaccine. Our data suggests that flu-ISCOMs may offer an improved vaccine strategy for protection of elderly humans against the complications of influenza infection.

PMID: 9223118 [PubMed - indexed for MEDLINE]

☐ **17:** Vaccine. 1996 Dec;14(17-18):1581-9. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Immune responses in mice induced by HSV-1 glycoproteins presented with ISCOMs or NISV delivery systems.

Hassan Y, **Brewer JM**, **Alexander J**, **Jennings R**.

Department of Medical Microbiology, University of Sheffield Medical School, UK.

The purpose of this study was to evaluate the immunogenicity of a herpes simplex virus type I (HSV-1) antigen preparation, obtained following zwitterionic detergent treatment of virus, and incorporation of the antigens into either immunostimulating complexes (ISCOMs) or non-ionic surfactant vesicles (NISV) delivery systems. Using Balb/c mice the ISCOM and NISV HSV-1 vaccines were assayed for their capacity to induce and enhance both the humoral and cellular immune responses, and to elicit protection against both homologous and heterologous virus challenge. The serum from animals vaccinated with either the NISV or the ISCOM HSV-1 antigen preparation, were found to contain high levels of total IgG and IgG1 and IgG2a subclass antibodies. In addition, both preparations were found to induce high neutralizing (NT) antibody levels following a two immunization protocol and to provide some protection against homologous and heterologous HSV challenge infection. Lymphoproliferative responses were observed in cultures of splenocytes from mice immunized with both HSV-1 NISV vaccine and HSV-1 ISCOMs vaccine, following various antigenic stimuli in vitro. In general, these were most marked in animals immunized with the HSV-1 NISV preparation, and particularly so when the splenocytes were stimulated in vitro with live HSV-1. Both the NISV and ISCOM HSV-1 vaccines were found to have induced interleukin 2, interleukin 10 and interferon-gamma in spleen cell culture supernatants, although again, the highest responses in general were observed in supernatant fluids from spleen cell cultures from animals immunized with the HSV-1 NISV preparation. These results suggest that a wide range of immune activity can be elicited by HSV-1 antigens presented to the immune system of mice in these formulations.

Publication Types:
- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 9032885 [PubMed - indexed for MEDLINE]

☐ **18:** J Gen Virol. 1995 Nov;76 (Pt 11):2707-15. Related Articles, Links

Full Text FREE J Gen Virol

Erratum in:
- J Gen Virol 1997 Feb;78(Pt 2):493.

Efficient replication of human immunodeficiency virus type 1 and measles virus in a human-to-mouse graft versus host disease model permits immunization research.

Huppes W, **Smit V**.

Health Research-TNO, HV Rijswijk, The Netherlands.

An acute graft versus host disease (GvHD) murine model was developed to study the pathogenic and

protective mechanisms against viruses that replicate in cells of the human immune system. The model allowed efficient replication of lymphotropic, macrophage and amphitropic strains of human immunodeficiency virus type 1 (HIV-1) and measles virus (MV). Cytopathic lymphotropic strains of HIV-1 and a wild-type MV strain replicated in a 'burst'-like manner, whereas a non-cytopathic lymphotropic HIV-1 strain and all macrophage-tropic HIV-1 strains caused persistent infection of the graft. The replication kinetics of infection with these viruses were highly reproducible and were very similar to those observed in natural infection of humans. Infection with these viruses, with the exception of HIV-1SF2, led to a delay [corrected] and abrogation of the GvHD, indicating a direct immunosuppressive effect. Interestingly, infection with the lymphotropic HIV-1SF2 strain was rapidly and spontaneously abrogated. The model was also shown to be suitable for the evaluation of passive immunization strategies. Administration of a combination of antibodies against the HIV-1 V3 loop and the HIV-1 CD4 binding sites prevented subsequent infection with HIV-1IIIB. In contrast, administration of CD4 binding site specific human monoclonal antibody at a concentration that would neutralize the virus in vitro enhanced in vivo infection with HIV-1IIIB. The model also allowed evaluation of in vivo immunization studies. Immunization with a live attenuated measles vaccine resulted in protection from a wild-type MV challenge, whereas immunization with a subunit candidate vaccine appeared to give partial protection.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 7595377 [PubMed - indexed for MEDLINE]

19: Vaccine. 1995 Feb;13(3):261-7. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Adjuvanticity of ISCOMs incorporating a T cell-reactive lipoprotein of the facultative intracellular pathogen Francisella tularensis.

Golovliov I, Ericsson M, Akerblom L, Sandström G, Tärnvik A, Sjöstedt A.

Department of Infectious Diseases, University of Umeå, Sweden.

Immunostimulating complexes (ISCOMs) are known to be highly effective adjuvants for envelope antigens of viral agents, but have not been evaluated for use with antigens of intracellular bacteria. Balb/c mice were subcutaneously immunized with ISCOMs into which the T cell-reactive membrane protein TUL4 of Francisella tularensis had been incorporated. Spleen cells from the immunized mice responded in vitro to TUL4 and to heat-killed F. tularensis live vaccine strain (LVS) with proliferation and production of gamma-interferon, whereas spleen cells from control mice immunized with TUL4 only did not respond to the antigens. When mice immunized with TUL4 ISCOMs were challenged with F. tularensis LVS, bacterial counts in spleen and liver were lower than in non-immunized mice. Again, TUL4 had no effect when used without ISCOMs. When proteins of a total membrane preparation of F. tularensis LVS were incorporated in ISCOMs and used for immunization, a decrease in bacterial counts was obtained which was similar in magnitude to that of TUL4 ISCOMs. Generally, the adjuvant effects demonstrated did not compare with the excellent protective effect of live tularaemia vaccine. Nonetheless, ISCOMs provide a means whereby protective antigens of F. tularensis can be tested.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 7631511 [PubMed - indexed for MEDLINE]

20: J Med Microbiol. 1995 Jan;42(1):53-61. Related Articles, Links

Full Text FREE J Med Microbiol

Comparative antibody responses and protection in mice immunised by oral or parenteral routes with influenza virus subunit antigens in aqueous form or incorporated into ISCOMs.

Ghazi HO, Potter CW, Smith TL, Jennings R.

Department of Experimental and Clinical Microbiology, University of Sheffield Medical School.

The total and subclass antibody responses of mice and protection of these animals against live influenza A/Sichuan/2/87 virus challenge infection were determined after immunisation with homologous A/Sichuan/87 aqueous or ISCOM-formulated surface glycoprotein subunit antigens administered by either the oral or intramuscular routes. The results show that the greatest systemic and local antibody responses were elicited in mice immunised with A/Sichuan ISCOMs by the intramuscular route; protection against homologous virus challenge was also effective in these animals, particularly after two doses of the vaccine. However, relatively high immune responses and protection were also elicited by the A/Sichuan/87 ISCOM vaccine administered orally. Immunisation of mice by the intramuscular route resulted in levels of serum IgG2a subclass antibody significantly greater than those induced by the same preparation given by the oral route, or by the aqueous A/Sichuan/87 subunit antigen preparation administered by either route. The findings indicate that the ISCOM delivery system can be used for immunisation by the oral route, although in mice, under the conditions used, this strategy compares unfavourably with the intramuscular route in terms of both local and systemic immune responses and protection against homologous challenge virus infection.

Publication Types:
- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 7739026 [PubMed - indexed for MEDLINE]

21: J Med Microbiol. 1994 Apr;40(4):261-9. Related Articles, Links

IgG subclass response and protection against challenge following immunisation of mice with various influenza A vaccines.

Ben-Ahmeida ET, Potter CW, Gregoriadis G, Adithan C, Jennings R.

Department of Experimental and Clinical Microbiology, University of Sheffield Medical School.

The serum total IgG and IgG subclass and nasal wash IgA and IgG antibody responses of mice to influenza virus A/Hong Kong/68 (H3N2) subunit preparations administered parenterally as a single dose, incorporated either in immune stimulatory compounds (ISCOMs) or liposomes with Freund's Complete Adjuvant, or as an aqueous material, as well as to live, infectious virus were measured by ELISA at 10 days and 3, 5, 7 and 22 weeks after immunisation. The protection of the upper and lower respiratory tracts provided by these preparations against homologous and heterologous challenge infection was assessed. Of the four variously-presented subunit preparations, influenza subunit ISCOMs induced relatively high and persisting levels of each of the different IgG subclasses, particularly IgG2a, throughout the study, and most nearly approached those observed after intranasal infection of mice with infectious virus. Furthermore, nasal wash IgA and IgG antibody levels, particularly at 5 or 7 weeks after immunisation, were also significantly greater in mice given the subunit ISCOM preparation than those induced by other subunit preparations with adjuvant or subunits given alone, and provided protection of both the upper and lower respiratory tracts against challenge as similar to that elicited by infectious virus.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 8151677 [PubMed - indexed for MEDLINE]

22: Virus Res. 1994 Apr;32(1):13-36. Related Articles, Links

An update on approaches to the development of respiratory syncytial virus (RSV) and parainfluenza virus type 3 (PIV3) vaccines.

Murphy BR, **Hall SL**, **Kulkarni AB**, **Crowe JE Jr**, **Collins PL**, **Connors M**, **Karron RA**, **Chanock RM**.

Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD.

RSV and PIV3 are responsible for about 30% of severe viral respiratory tract disease leading to hospitalization of infants and children. For this reason, there is a need to develop vaccines effective against these viruses. Since these viruses cause severe disease in early infancy, vaccines must be effective in the presence of maternal antibody. Currently, several strategies for immunization against these viruses are being explored including peptide vaccines, subunit vaccines, vectored vaccines (e.g., vaccinia-RSV or adenovirus-RSV recombinants), and live attenuated virus vaccines. The current status of these approaches is reviewed. In addition, the immunologic basis for the disease potentiation seen in vaccinees immunized with formalin-inactivated RSV during subsequent RSV infection is reviewed. The efficacy of immunization in the presence of maternal antibody is discussed. Much progress for a RSV and PIV3 vaccine has been made and successful immunization against each of these pathogens should be achieved within this decade.

Publication Types:
- Review

PMID: 8030364 [PubMed - indexed for MEDLINE]

☐ **23:** Vaccine. 1993 Oct;11(13):1302-9. Related Articles, Links

Immunopotentiation of local and systemic humoral immune responses by ISCOMs, liposomes and FCA: role in protection against influenza A in mice.

Ben Ahmeida ET, **Gregoriadis G**, **Potter CW**, **Jennings R**.

Department of Experimental and Clinical Microbiology, University of Sheffield Medical School, UK.

The immunogenicity and protective efficacy of an influenza A subunit vaccine preparation administered to mice in an aqueous form, or presented as immunostimulatory complexes (ISCOMs), liposomes or with Freund's complete adjuvant (FCA), were assessed in comparative studies with live infectious virus. Both intranasal and parenteral routes of administration were assessed. An enzyme-linked immunosorbent assay (ELISA) was used to measure nasal wash and serum antibody responses in groups of unprimed mice, while protection was determined by the recovery of homologous influenza virus from mouse nasal washes and lung homogenates following challenge infection by the intranasal route. The results showed that parenteral administration of the influenza antigen preparations induced variable levels of both local and systemic antibodies at weeks 3, 7 and 22 postimmunization. Although the overall greatest levels of antibody and protection were elicited in mice following live virus infection, formulation of influenza surface haemagglutinin (HA) and neuraminidase (NA) proteins into ISCOMs elicited high and persistent antibody responses and provided relatively good protection of the upper and lower respiratory tracts of these animals. The results also show a relatively poor effect of the subunit antigen preparations in promoting humoral immune responses and protection irrespective of the nature of their presentation, when given by the intranasal route.

Publication Types:
- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 8296483 [PubMed - indexed for MEDLINE]

☐ **24:** Vet Immunol Immunopathol. 1993 Jul;37(2):165-80. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Local antibody forming cell responses to the Hitchner B1 and Ulster strains of Newcastle disease virus.

Russell PH, **Koch G**.

Department of Veterinary Pathology, Royal Veterinary College, London, UK.

The Hitchner B1 and Ulster strains of Newcastle disease virus (NDV) replicated to high titre in the Harderian gland (HG) after eye-drop infection. The Harderian gland then became the major site of antiviral IgA-antibody-forming cells (AFC) in the body and their number correlated to the level of antiviral IgA antibody in the tears. The spleen, HG and femoral bone marrow all contained comparable levels of antiviral IgG-AFC and IgM-AFC after two intra-ocular inoculations of virus, whereas the caecal tonsil and bursa contained few AFC despite the local replication of the Ulster strain of NDV leading to high titres of virus in the faeces. Vaccines of the Hitchner B1 strain of NDV were much less effective at inducing antibody by the intranasal compared with intra-ocular route and no virus was re-isolated after intranasal vaccination. The intravenous inoculation of inactivated Iscoms of NDV could stimulate the spleen, but not the Harderian gland to the same extent as a live virus.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 8236795 [PubMed - indexed for MEDLINE]

25: Scand J Infect Dis Suppl. 1993;88:103-8. Related Articles, Links

High yield production of an inactivated coxsackie B3 adjuvant vaccine with protective effect against experimental myocarditis.

Fohlman J, **Pauksen K**, **Morein B**, **Bjare U**, **Ilbäck NG**, **Friman G**.

Dept of Infectious Diseases, University Hospital, Uppsala, Sweden.

Dilated cardiomyopathy, perhaps chronic postviral fatigue syndrome as well as juvenile diabetes could be triggered by enteroviral infections. The frequency of sudden death after myocarditis and its relationship to enteroviral infections is disputed. Neonatal enteroviral disease is rare, but can be severe. It is also possible that enteroviruses pose a threat to immunocompromised patients, like bone marrow transplant recipients. Consequently, the emergence of chronic enteroviral diseases as a concept, prompted our attempts to produce an enteroviral vaccine. 1. Live attenuated enterovirus strains were previously in some cases shown to be suitable as vaccine candidates. We obtained neutralizing antibody titres ranging from 40-2560 against Coxsackie B3 virus (RD strain). Animals were protected to 90% against challenge infection. 2. Inactivated whole vaccine. We used beta-propiolactone to inactive Coxsackie B3 virus. 74% of the animals survived if the vaccine was prepared with Quil A matrix as adjuvant. The neutralisation antibody titres varied from < 5 to 320. By comparison aluminium hydroxide ($p = 0.06$) and Freund's adjuvant were inferior ($p < 0.01$). 3. Subunit vaccines. We have previously used the ISCOM (immunostimulatory complex) technology to produce a Coxsackie B3 subunit vaccine. High levels of neutralizing antibodies were obtained (512)-comparable to natural infection. All animals survived challenge infection after two booster doses with 16 nanogram of the ISCOM preparation. Limiting for this technique was the availability to include sufficient amount of antigenic protein material. In addition to neutralizing antibodies a cellular response might be obtainable. In conclusion we have shown that vaccine can be made against Coxsackie B3 virus with good protective effect and significant neutralisation antibody titre. (ABSTRACT TRUNCATED AT 250 WORDS)

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 8390713 [PubMed - indexed for MEDLINE]

26: J Exp Med. 1992 Jul 1;176(1):119-28. Related Articles, Links

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Measles virus transmembrane fusion protein synthesized de novo or presented in

immunostimulating complexes is endogenously processed for HLA class I- and class II-restricted cytotoxic T cell recognition.

van Binnendijk RS, van Baalen CA, Poelen MC, de Vries P, Boes J, Cerundolo V, Osterhaus AD, UytdeHaag FG.

Laboratory of Immunobiology, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

The routes used by antigen-presenting cells (APC) to convert the transmembrane fusion glycoprotein (F) of measles virus (MV) to HLA class I and class II presentable peptides have been examined, using cloned cytotoxic T lymphocytes in functional assays. Presentation by Epstein-Barr virus-transformed B lymphoblastoid cell lines was achieved using live virus, ultraviolet light-inactivated virus, and purified MV-F delivered either as such or incorporated in immunostimulating complexes (MV-F-ISCOM). Only live virus and MV-F-ISCOM allow presentation by class I molecules, while all antigen preparations permit class II-restricted presentation. We observe presentation of MV-F from live virus and as MV-F-ISCOM by class II molecules in a fashion that is not perturbed by chloroquine. Our studies visualize novel presentation pathways of type I transmembrane proteins.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 1613454 [PubMed - indexed for MEDLINE]

PMCID: PMC2119300

27: Arch Virol. 1992;125(1-4):71-86. Related Articles, Links

The IgA and subclass IgG responses and protection in mice immunised with influenza antigens administered as ISCOMS, with FCA, ALH or as infectious virus.

Ben Ahmeida ET, Jennings R, Erturk M, Potter CW.

Department of Experimental and Clinical Microbiology, University of Sheffield Medical School, U.K.

Comparative studies on the local IgA, and circulating IgG subclass antibody responses of mice to A/Sichuan/2/87 (H3N2) influenza virus surface antigens administered with different carrier or delivery systems by the parenteral route, were carried out. The results obtained were compared with the responses observed following live influenza virus infection, and the protection afforded to these animals by these various preparations determined. Infection with live virus elicited early and high levels of protection against homologous virus challenge and this correlated with both local IgA and circulating IgG2a antibody levels. When incorporated into immunostimulating complexes (ISCOMS), A/Sichuan surface antigens promoted high levels of local IgA and circulating IgG1 antibody, and achieved a more rapid and more solid immunity against homologous virus challenge infection, than that elicited by the same surface antigens administered alone or together with Freund's complete adjuvant or alhydrogel.

PMID: 1642561 [PubMed - indexed for MEDLINE]

28: Vaccine. 1992;10(2):107-12. Related Articles, Links

Initiation of cytotoxic T-cell response and protection of Balb/c mice by vaccination with an experimental ISCOMs respiratory syncytial virus subunit vaccine.

Trudel M, Nadon F, Séguin C, Brault S, Lusignan Y, Lemieux S.

Centre de recherche en virologie, Institut Armand-Frappier, Université du Québec, Laval, Canada.

Respiratory syncytial virus is an important human pathogen causing serious lower respiratory tract infections of children and elderly people. Previous studies on the development of experimental subunit

vaccines either expressed by recombinant DNA technology or prepared from purified viral proteins absorbed on adjuvant (ISCOMs) have shown promise. The present work reports on the effectiveness of an experimental ISCOMs vaccine in initiating humoral and cell-mediated immune responses and in providing overall protection upon live virus challenge in Balb/c mice; results indicate that vaccination by the intramuscular route is more effective, even if vaccination by the intranasal route also significantly reduced virus shedding.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 1539463 [PubMed - indexed for MEDLINE]

29: AIDS Res Hum Retroviruses. 1991 Mar;7(3):271-7. Related Articles, Links

Vaccine protection against HIV-2 infection in cynomolgus monkeys.

Putkonen P, Thorstensson R, Walther L, Albert J, Akerblom L, Granquist O, Wadell G, Norrby E, Biberfeld G.

Department of Immunology, National Bacteriological Laboratory, Stockholm, Sweden.

The aim of this study was to determine if protection against an infectious human immunodeficiency virus type 2 (HIV-2) challenge could be obtained in cynomolgus macaques by active immunization using whole killed virus vaccine. Four monkeys were immunized with killed HIV-2SBL-6669, two of them with five intramuscular (im) injections of viral preparation containing 100 or 300 micrograms protein emulsified in incomplete Freund's adjuvant (IFA) and the two remaining received four im injections of 25-50 micrograms viral protein in iscoms. Each of the four vaccinated cynomolgus monkeys, along with four unvaccinated controls, were challenged intravenously two weeks after the last booster with approximately 100 animal infectious doses (ID50) of live HIV-2SBL-6669. All four immunized monkeys developed antibodies to HIV-2 envelope and core proteins before challenge exposure to HIV-2, but only the two animals vaccinated with virus in IFA developed detectable neutralizing antibodies. The two monkeys immunized with killed virus in IFA have shown no evidence of infection nine months after challenge with live virus. When blood and lymph node cells from these animals were transfused into naive cynomolgus monkeys, the recipients remained free of infection. In contrast, virus was recovered repeatedly in all nonimmunized animals and in the two animals immunized with iscom-associated viral antigens, which had a low content of envelope gp125 antigen. The demonstration of vaccine-induced protection against HIV-2 in a nonhuman primate raises hope for effective immunization against HIV infections in humans as well.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 2064826 [PubMed - indexed for MEDLINE]

30: Vaccine. 1989 Feb;7(1):12-6. Related Articles, Links

Experimental polyvalent ISCOMs subunit vaccine induces antibodies that neutralize human and bovine respiratory syncytial virus.

Trudel M, Nadon F, Séguin C, Simard C, Lussier G.

Centre de Recherche en Virologie, Institut Armand-Frappier, Université du Québec, Ville de Laval, Canada.

The purpose of the present study was to evaluate experimentally, in guinea-pigs, the immunogenicity of respiratory syncytial (RS) virus subunit vaccines. Immunostimulating complexes (ISCOMs), made from the surface proteins of both human (Long) and bovine (A-51908) RS strains adsorbed to the adjuvant Quil A, were assayed for their capacity to induce neutralizing antibodies, in comparison to experimental live virus vaccines. Serums from animals vaccinated with either the human or bovine RS subunit vaccines

were equally efficient in neutralizing human or bovine RS virus. ISCOMs prepared with bovine RS virus proteins were significantly (p less than 0.05%) more efficient than their human counterpart, in inducing neutralizing antibodies, suggesting their greater potential as a subunit vaccine.

Publication Types:
- Research Support, Non-U.S. Gov't

PMID: 2718604 [PubMed - indexed for MEDLINE]

31: Can J Microbiol. 1988 Dec;34(12):1351-4. Related Articles, Links

Neutralizing response of rabbits to an experimental rubella subunit vaccine made from immunostimulating complexes.

Trudel M, **Nadon F**, **Séguin C**, **Payment P**.

Centre de recherche en virologie, Université du Québec, Ville de Laval, Canada.

The purpose of this study was to evaluate experimentally the immunogenicity in rabbits of rubella subunits adsorbed to the adjuvant Quil A. The adsorbed viral proteins form structurally defined ImmunoStimulating COMplexes (ISCOMs). Rubella ISCOMs were tested for their capacity to induce neutralizing and hemagglutination-inhibiting antibodies, in comparison with a commercial live attenuated vaccine. Rubella ISCOMs were as efficient as the live vaccine in inducing neutralizing and hemagglutination inhibiting antibodies, suggesting the possibility of developing an ISCOMs subunit vaccine.

Publication Types:
- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 3233560 [PubMed - indexed for MEDLINE]

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